

PCT/EP00/06271

Max-Planck-Gesellschaft zur Förderung der....

Our Ref.: D 1920 PCT

CLAIMS

1. A method for the selection of at least one member of a number of specifically interacting molecules from libraries, said method comprising as the first step involving the contact of said interacting molecules:
 - (a) contacting a first molecule with a second molecule affixed to a magnetic particle under conditions that allow a specific interaction between said first and second molecule to occur;

and further the steps of:

 - (b) subjecting the product obtained in step (a) to at least one washing step;
 - (c) determining whether a specific interaction between said first and second molecule had occurred; and, if said specific interaction had occurred,
 - (d) providing said first and/or second molecule selected by steps (a) to (c), wherein steps (a), (b) and (c) are carried out in parallel in (a) container(s) preferably representing an arrayed form, e.g. in (a) microtiter plate(s), using an automated device comprising a magnetic particle processor.
2. The method of claim 1, wherein said first and/or second molecule is an organic molecule and/or a mixture of organic molecules and/or inorganic molecules.
3. The method of claim 1 or 2, wherein said first and/or second molecule is a hapten.
4. The method of claim 2 or 3, wherein said first and/or second molecule is a cDNA expression product, and/or a (poly)peptide, and/or a nucleic acid, and/or a lipid, and/or a sugar, and/or a steroid, and/or a hybrid of said molecules.
5. The method of claim 4, wherein said cDNA expression product is an antibody or a fragment or a derivative thereof, an enzyme or a fragment

thereof, a surface protein or a fragment thereof, or a nucleic acid-binding protein or a fragment thereof.

6. The method of any one of claims 1 to 5, wherein said first molecule is a (poly)peptide presented on the surface of organisms (e.g. phage, viruses, bacteria, eukaryotic cells) and/or organelles (e.g. ribosome) and/or soluble molecules (e.g. nucleic acids, protein-nucleic acid hybrids) and wherein the method further comprises after step (b) and prior to step (c) the step of:
(b') amplifying a (poly)peptide specifically interacting with said second molecule,
wherein step (b') is carried out in (a) container(s) preferably representing an arrayed form, e.g. in (a) microtiter plate(s).
7. The method of claim 6, wherein prior to step (a) said library of first molecules (library 1) is preabsorbed with unloaded magnetic particles and/or molecules competitive (cross-reactive) to second molecules (target, library 2).
8. The method of claim 6 or 7 which further comprises after step (c) and prior to step (d) the step of:
(c') repeating steps (a), (b) and (c) and, optionally, step (b') at least once.
9. The method of claim 8, wherein steps (c) and (c') are performed in parallel.
10. The method of any one of claims 1 to 9, wherein said number of specifically interacting molecules is a pair of interacting molecules.
11. The method of any one of claims 1 to 9, wherein said number of specifically interacting molecules are three or more interacting molecules.
12. The method of any one of claims 1 to 11 further comprising the step of characterizing said first and/or second molecule and/or the corresponding genetic information.

13. The method of any one of claims 1 to 12, wherein said second molecule target is affixed to said magnetic particle via an affinity tag (e.g. a metal-chelating tag, an epitope tag, an enzyme binding domain, calmodulin, biotin, Strep-tag, protein A, protein G or protein L) and/or unspecific adsorption (e.g. plastic surface) and/or covalent binding (e.g. via functional groups such as NH₂-, COOH-, SH-groups).
14. The method of claim 13, wherein said metal-chelating tag is a His-tag, and/or said epitope tag is an HA-tag, a c-myc-tag, a VSV-G-tag, an α -tubulin-tag, a B-tag, an E-tag, FLAG, a His-tag, an HSV-tag, a Pk-tag, a protein C-tag, a T7-tag, EpiTagTM, a V5-tag or an S-tag, and/or said enzyme binding domain is cellulose binding domain, barnase or maltose binding protein.
15. The method of any one of claims 1 to 14, wherein step (c) is effected by immunological means.
16. The method of claim 15, wherein step (c) is effected by ELISA, RIA, western/colony blotting, FACS or immunohistochemistry.
17. The method of claim 15 or 16, wherein step (c) is effected in (micro-)array format, preferably on a membrane and/or filter and/or a glass slide and/or in a microtiter plate.
18. A method for the production of a pharmaceutical composition comprising the steps of the method of any one of claims 1 to 17 and further the step of formulating said first and/or second molecule selected and/or characterized by the method of any one of claims 1 to 17 or a functionally and/or structurally equivalent derivative thereof in a pharmaceutically acceptable form.